American Journal of Hematology 56:52–58 (1997)

Magnetic Resonance Imaging of Reticulo-Endothelial System in Patients With Idiopathic Thrombocytopenic Purpura

S. Morio,[1] H. Oh,[1]* N. Endo,[1] E. Kawano,[1] H. Nakamura,[1] T. Asai,[1] Y. Saito,[1] Y. Uchida,[2] H. Ikehira,[2] and K. Yoshida[3]

[1]Second Department of Internal Medicine, School of Medicine, Chiba University, Chiba City, Chiba, Japan
[2]Department of Radiology, School of Medicine, Chiba University, Chiba City, Chiba, Japan
[3]National Institute of Radiological Sciences, Chiba City, Chiba, Japan

Idiopathic thrombocytopenic purpura (ITP) is characterized by accelerated platelet destruction in the reticulo-endothelial system (RES). We performed magnetic resonance imaging (MRI) to estimate the degree of activated RES. MRI was performed with a Gyroscan S-15 (1.5 tesla) in 7 healthy volunteers and 22 patients with ITP. The 22 patients included 19 who were at initial diagnosis or were nonresponders to the therapy (non-DX group), and 3 who were responders. For the non-DX group, the T1 relaxation time of the spleen was initially significantly shorter than for healthy volunteers, but normalized after responding to the therapy. The initially shorter T1 values of the spleen for ITP patients correlated with a low platelet count ($P < 0.05$). This condition may indicate foam cells or fatty components due to platelet destruction. There was no significant relationship between the sequestration in ^{111}In-scan and T1 values of the liver or spleen. However, MRI is a noninvasive method, and it may be a clinically useful tool in the evaluation of RES in patients with ITP. Am. J. Hematol. 56:52–58, 1997.

Key words: MRI; reticulo-endothelial system; ITP

INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disorder caused by the destruction of platelets in the reticulo-endothelial system (RES). Platelet destruction is caused by the binding of circulating anti-platelet antibodies [1,2]. Platelet kinetic studies have been performed by the ^{51}Cr labeling technique [3,4] or the ^{111}In Labeling technique [5,6] to analyze the site of platelet sequestration. The ^{111}In technique has been more commonly used than the ^{51}Cr technique, because of its shorter half-life and high affinity to the platelets.

Recently, magnetic resonance imaging (MRI) has been used for the imaging of bone marrow (BM) in patients with aplastic anemia or leukemia [7–9]. MRI is also known to be very useful for determining the amount of fat and cells in bone marrow. In our study, we utilized MRI to evaluate platelet destruction or pooling in RES.

MATERIALS AND METHODS

Seven healthy volunteers (age range, 26–46 years; mean, 35 years) and 22 patients with ITP were studied. Characteristics of the patients are shown in Table I. The patients included 19 who were at initial diagnosis or were nonresponders to the therapy (non-DX group) (age range, 17–73 years; mean, 42.6 years), and 3 who were responders (age range, 22–66 years; mean, 45.0 years). Two of 3 responders were also examined before the treatment.

^{111}In platelet kinetics were performed in 12 patients of the non-DX group. Autologous platelets from specimens of 50–100 ml of ACD-anticoagulated blood were isolated by differential centrifugation, labeled with ^{111}In-

*Correspondence to: Hakumei Oh, M.D., Department of Medicine, Chiba University School of Medicine, 1-16, Shindencho, Chuo-ku, Chiba 260, Japan.

Received for publication 31 May 1996; Accepted 7 May 1997.

TABLE I. Characteristics of 22 Patients With ITP*

No.	Age/sex	Duration of disease (months)	Previous treatment[a]	Plt ($\times 10^4$ μl)	PAIgG (ng/10^7 cells)	Plt survival (days)	In-scan type[b]
ITP (non-Dx)							
Initial diagnosis							
1	42/F	4.0		5.9	138.0	1.5	M
2	33/M	1.0		1.5	178.1	2.5	M
3	20/F	17.0		5.2	289.1	ND	ND
4	27/F	7.0		7.0	231.0	ND	ND
5	58/M	6.0		2.0	ND	ND	ND
6	66/F	38.0		1.2	189.0	0.4	H
7	53/F	2.0		3.3	132.5	1.08	S
8	22/M	1.0		1.0	370.3	3.5	M
9	39/F	18.0		5.3	42.7	0.6	S
Nonresponder							
10	26/F	45.0	PSL	1.6	93.1	0.7	M
11	49/F	80.0	PSL, CyA, DZ, NT, Co, VA	2.1	131.0	0.4	S
12	73/F	108.0	PSL, DZ	2.0	23.8	ND	ND
13	44/M	34.0	PSL, NT, VA	3.3	349.8	ND	ND
14	53/F	27.0	Co, NT	5.6	150.6	ND	ND
15	28/F	58.0	DZ, VA, Co	3.4	64.0	ND	ND
16	48/F	1.5	CyA	1.9	246.4	2.35	H
17	65/M	28.0	Co, NT	2.7	285.9	0.5	M
18	47/F	36.0	PSL	3.1	289.6	1.5	S
19	17/F	36.0	PSL	3.0	108.5	0.45	S
ITP (responder, R)							
1	66/M	13.0	PSL	14.0	ND	ND	ND
2 (8)[c]	22/M	2.0	PSL	24.6	18.2	ND	ND
3 (18)[c]	47/F	39.0	PSL	9.9	ND	ND	ND

*ND, not done.
[a]PSL, prednisolone; CyA, cyclosporin A; DZ, danazol; NT, neurotropin; Co, colchicine; VA, vinca alkaloid.
[b]M, mixed type; H, hepatic type; S, splenic type.
[c]Same patient in non-Dx group.

Fig. 1. Coronal MR image from the T1 calculating method. Regions of interest (ROI) with the numbers 28–30 are placed in the bone marrow, liver, and spleen, respectively.

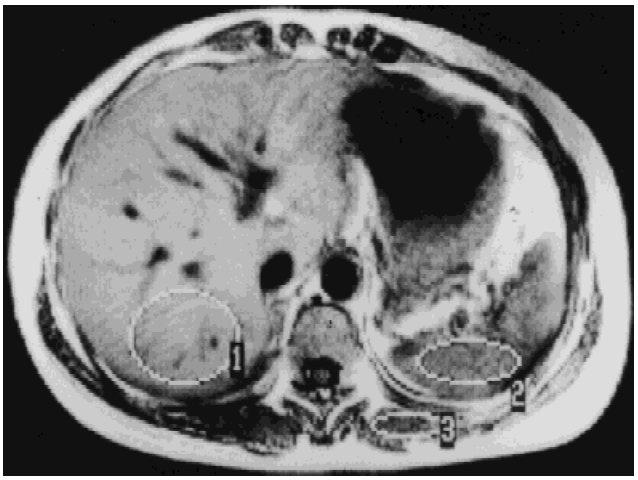

Fig. 2. Transverse MR image from T1-weighted spin-echo method. ROI with the numbers 1–3 are placed in the liver, spleen, and muscle, respectively.

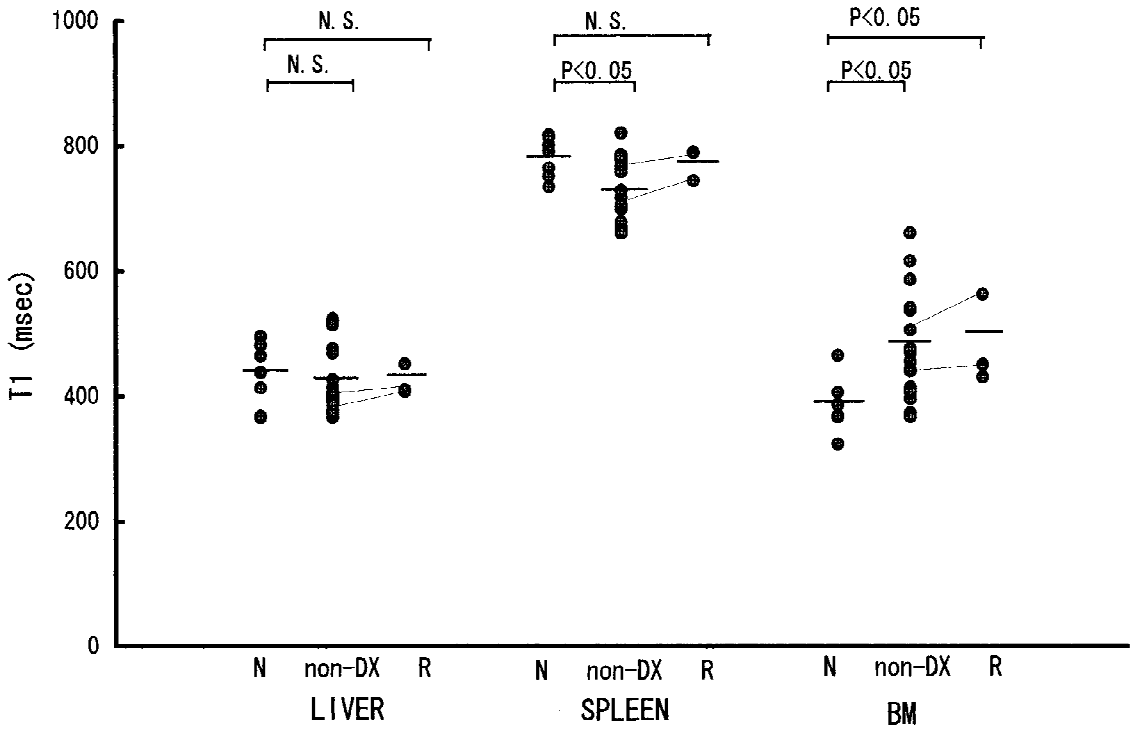

Fig. 3. T1 relaxation times of the liver, spleen, and bone marrow. Mean T1 value of the spleen in the non-DX group is significantly shorter than in the control. Mean T1 value of the bone marrow in the ITP group is significantly longer than in the control. The change in the same patient's data is shown by the line. N, normal (n = 7); non-DX, ITP patient at initial diagnosis or nonresponder to therapy (n = 19); R, responder (n = 3).

tropolone, and reinjected [5]. The ^{111}In radioactivities in the liver and spleen were quantitatively assessed with a computerized gamma camera system 24 hr after injection of the platelets. Predominantly splenic and hepatic sequestration was defined as a spleen/liver ratio of >4.5 and <2.5; mixed sequestration was defined as a ratio from 2.5–4.5. Blood samples were obtained daily for a week and the radioactivities were measured by a gamma counter to calculate platelet lifespan.

MRI was performed on a 1.5-tesla superconductive MR-imaging system (Gyroscan S-15, Philips). The patients were placed in a supine position in the scanner. The field of view was 40 cm, and the matrix size was 256 × 256.

The imaging for calculating T1 relaxation times was obtained from a coronal section with 217 8-mm-thick slice by body coil with a repetition time (TR) of 800 and 2,200 msec and an echo time (TE) of 20 msec. The circular regions of interest (ROI) were placed in the liver or spleen, and the square ROI in the lumbar vertebral marrow space (Fig. 1). The mean T1 values were calculated from the average of three ROI.

In 12 cases, transverse T1-weighted images were obtained in contiguous 8-mm slices in a 256 × 256 matrix with TR = 600 msec, TE = 15 msec. Measurements of signal intensity in the liver, spleen, and bone marrow were obtained from the average of three ROI. The ratios of signal intensity (SI ratio) were then calculated with respect to the muscle (Fig. 2).

The significance of the difference between mean T1 or SI ratio of the two groups was performed by Student's unpaired t-test.

RESULTS

The T1 values for the normal and the patient groups are shown in Figure 3. All T1 values were not affected by age or sex (not shown). In the non-DX group of ITP patients, no significant difference was detected between initial diagnosis and nonresponder, respectively, liver (mean ± SD), 443.6 ± 63.6 vs. 405.8 ± 29.3 msec; spleen, 734.1 ± 45.0 vs. 737.1 ± 52.4 msec; and BM, 491.0 ± 96.8 vs. 455.8 ± 69.5 msec. Therefore, these analyses were done together as a non-DX group.

T1 values of the liver were not significantly different between the group of normal individuals, the group of non-DX patients, and the group of responders (432.7 ± 52.1, 423.5 ± 51.2, and 423.7 ± 24.6 msec, respectively). T1 values of the spleen were originally shorter for the non-DX group (735.7 ± 47.7 msec) than for the normal group (782.3 ± 32.2 msec) ($P < 0.05$). In particular, 7 patients with severe thrombocytopenia (platelet count $\leq 2 \times 10^4/\mu 1$) in the non-DX group showed markedly

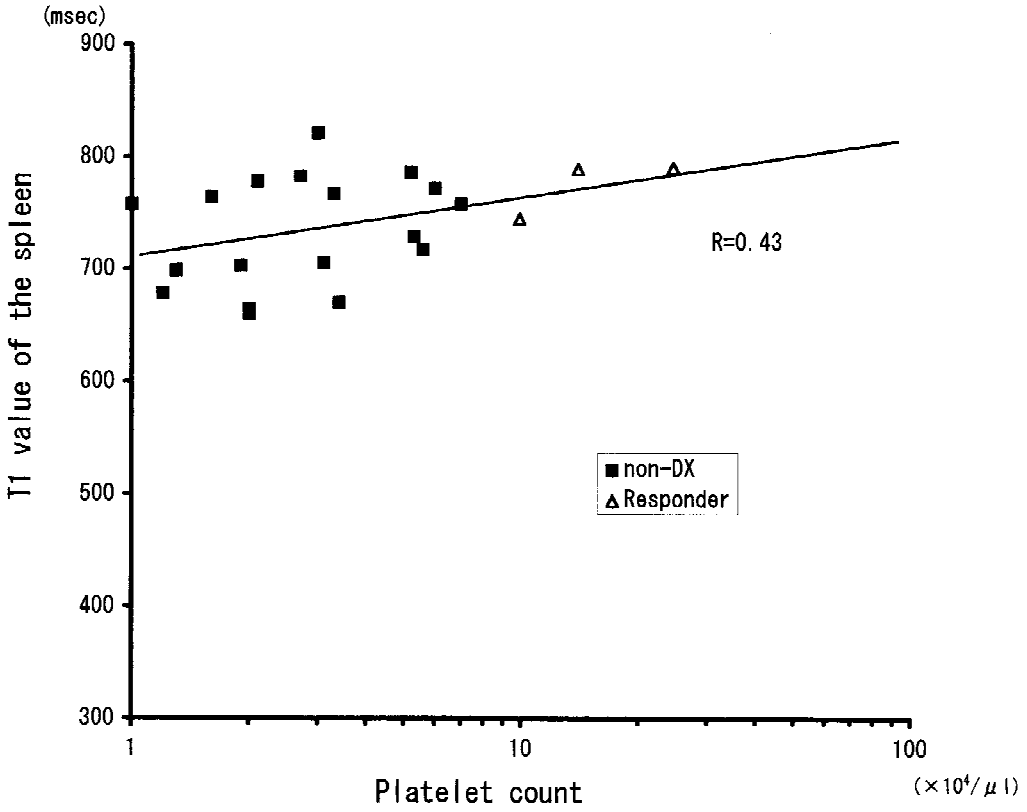

Fig. 4. Relationship between T1 values of spleen and platelet counts in patients with ITP. T1 value shows a linear relationship to platelet count ($P < 0.05$). ■, non-DX (n = 19); △, responder (n = 3).

short T1 values of the spleen (703.8 ± 42.2 msec) as compared with the normal group ($P < 0.005$). These short T1 values were normalized (774.6 ± 26.0 msec) after responding to therapy. The change in the same patient's data is shown by the line in Figure 3.

T1 values of the bone marrow were longer for the non-DX group (472.5 ± 83.1 msec) and responders (481.5 ± 71.5 msec) than for the normal group (386.2 ± 47.3 msec) ($P < 0.05$).

When we examined the relationship between T1 values and the platelet counts in the patients, a significant correlation was apparent between T1 values of the spleen and the platelet counts ($P < 0.05$), as shown in Figure 4.

On the other hand, the SI ratios of the liver, spleen, and bone marrow were not significantly different between the three groups (Fig. 5).

Figure 6 shows the relationship between the sequestration type in the ^{111}In-scan and the T1 values of the spleen or liver. No significant correlation was detected; however, the two cases of liver type showed a very short T1 value for both the liver and the spleen. Platelet lifespans were shorter for the non-DX group (mean 1.35 days, range 0.4–3.5 days), which had no significant relation to the T1 values of the spleen or liver.

DISCUSSION

MRI provides a noninvasive and useful means to evaluate large portions of bone marrow because of the different proton NMR relaxation properties of fatty and cellular tissues. T1-weighted spin-echo or STIR (short time-interval inversion recovery) imaging has usually been applied to qualitative evaluation of bone marrow [7,10–12]. In aplastic anemia, the typical fatty marrow shows a bright signal in T1-weighted images and no signal in STIR images. Moreover, the measurements of T1 relaxation times in bone-marrow disorders have been reported as short T1 in aplastic anemia and long T1 in leukemia [8,9,13,14].

In the present study, we measured T1 values and SI ratios from T1-weighted images for RES imaging of ITP patients. Although the T1 value of the spleen was lower in the non-DX group than in the normal group, SI ratios were inconclusive. In addition, the T1 measurements were superior in signal intensity to T1-weighted images, as previously reported [9].

The short T1 values in the spleen suggested an increase in the fatty elements in the spleen. Previous pathological studies for ITP spleens revealed that macrophages phagocytosed many existing platelets and foamy cells

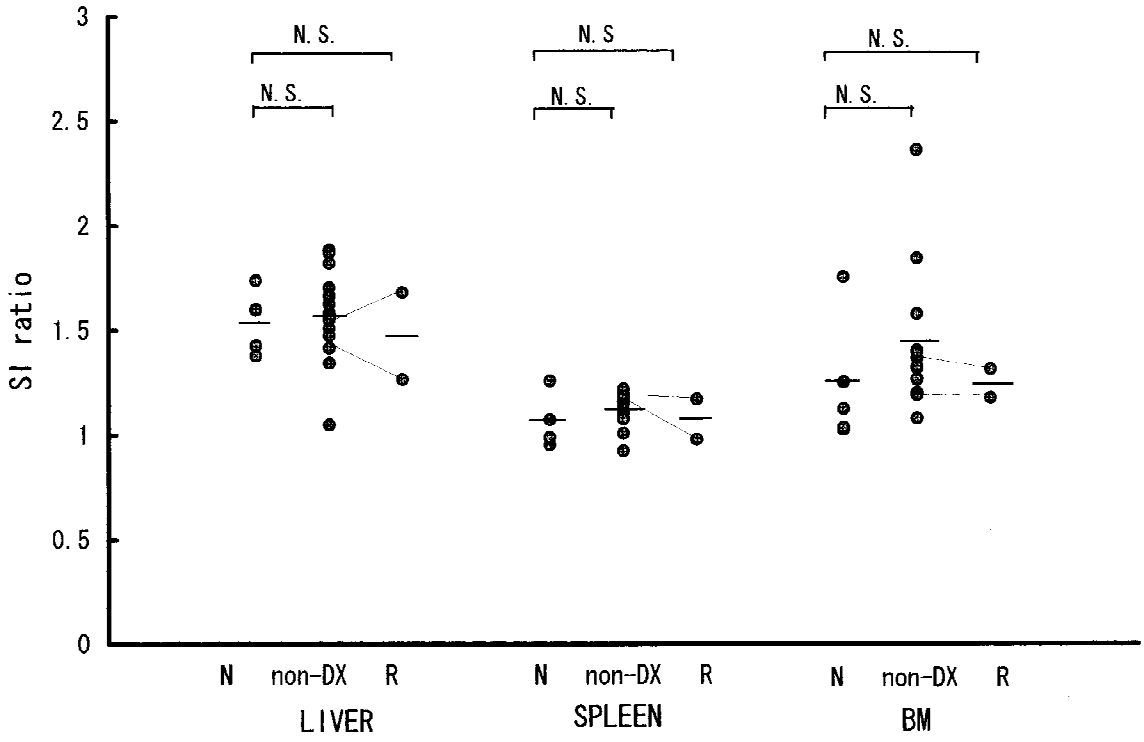

Fig. 5. Signal intensity (SI) ratios of the liver, spleen, and bone marrow. No significant differences are shown. The change in the same patient's data is shown by the line. N, normal (n = 5); non-DX, (n = 14); R, responder (n = 2).

[15,16]. Foamy cells have been considered as the macrophages which contain phospholipids derived from platelet membranes beyond the capacity of lysosomal digestion [17]. The increase of fatty elements by the destruction of platelets and foamy cells could be clearly observed with MRI. T1 values of the spleen in ITP patients were significantly correlated with platelet counts, and the short T1 value was thought to reflect the severity of ITP. Since splenectomies have not been performed in all our cases, pathological findings have not been obtained. Further studies of STIR imaging and pathological examination are planned to confirm these results.

Splenectomy is usually indicated for chronic ITP patients if steroids have failed or if patients are developing serious side effects. The useful prognostic factors for splenectomy have been discussed in many reports: age [18], platelet survival [19], previous response to steroids [20], and sequestration site [18,21,22]. Some workers have reported lack of useful predictors [23].

Although ^{111}In-labeled platelet kinetics were performed in 12 patients in this study, no significant correlation was observed between sequestration types and MRI values. However, two predominantly hepatic cases revealed short T1 relaxation times for both the spleen and liver, so these cases might indicate that platelets were rapidly destroyed in RES. The difference between ^{111}In-scan and MRI might be due to the fact that the platelet-labeling method consists of measuring the *relative* radioactivity of the liver and spleen, compared to the *absolute* MRI values. Secondly, the spleen is a major site of autoantibody synthesis in ITP [2,24], which might yield some influence on MRI values of the spleen.

On the other hand, long T1 relaxation times of the bone marrow were observed in patients with ITP. These long T1 values may be related to the increase of megakaryocytes in the bone marrow.

A preliminary MRI study was performed on 3 patients with essential thrombocythemia (ET) and on 2 patients with chronic myelogenous leukemia (CML). All 5 patients had a splenomegaly, and the platelet count increased from 98.0 to 225.2 (mean, 168.3) $\times 10^4/\mu$l. Although the T1 value of the liver (463.4 ± 36.3 msec) was not different from that in normal and ITP patients, the T1 value of the spleen was longer for ET/CML (815.8 ± 31.2 msec) than for the ITP non-DX group (735.7 ± 47.7 msec) ($P < 0.01$). The T1 value of the BM was also longer for ET/CML (541.0 ± 95.4 msec) than for the normal (386.2 ± 47.3 msec) and ITP non-DX group (472.5 ± 83.1 msec) ($P < 0.05$). The prolonged T1 value of the spleen and BM in ET/CML may be due to the increase of cellular components by the proliferation of platelets and myeloid cells.

A large number of studies on patients with ITP and other diseases will be helpful in verifying the usefulness of MRI for RES.

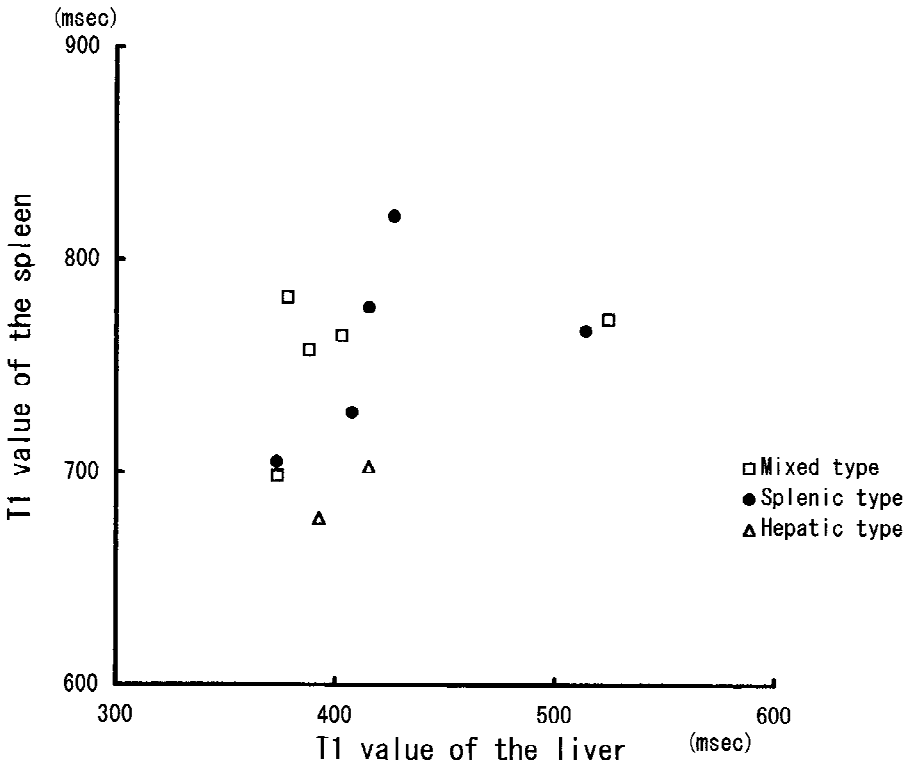

Fig. 6. Relationship between T1 value of the spleen/liver and the sequestration type in ^{111}In-scan (n = 12). No significant correlation is observed. ●, splenic type; △, hepatic type; □, mixed type.

CONCLUSIONS

Based on our findings of the decrease in T1 values of spleens of patients with ITP, and on the proven noninvasiveness of MRI, MRI may be a clinically useful tool in the evaluation of RES in patients with ITP.

REFERENCES

1. Karpatkin S: Autoimmune thrombocytopenic purpura. Blood 56:329–343, 1980.
2. McMillan R: Chronic idiopathic thrombocytopenic purpura. N Engl J Med 304:1135–1147, 1981.
3. Harker LA, Finch CA: Thrombokinetics in man. J Clin Invest 48:963–974, 1969.
4. International Committee for Standardization in Hematology (ICSH): Recommended methods for radioisotope platelet survival studies. Blood 50:1137–1144, 1977.
5. Dewanjee MK, Rao SA, Didisheim P: Indium-111 tropolone, a new high-affinity platelet label: Preparation and evaluation of labeling parameters. J Nucl Med 22:981–987, 1981.
6. International Committee for Standardization in Hematology (ICSH): Recommended method for Indium-111 platelet survival studies. J Nucl Med 29:564–566, 1988.
7. Olson DO, Shields AF, Schuerich CJ, Porter BA, Moss AA: Magnetic resonance imaging of the bone marrow in patients with leukemia, aplastic anemia, and lymphoma. Invest Radiol 21:540–546, 1986.
8. McKinstry CS, Steiner RE, Young AT, Jones L, Swirsky D, Aber V: Bone marrow in leukemia and aplastic anemia: MR imaging before, during, and after treatment. Radiology 162:701–707, 1987.
9. Smith SR, Williams CE, Davies JM, Edwards RHT: Bone marrow disorders: Characterization with quantitative MR imaging. Radiology 172:805–810, 1989.
10. Cohen MD, Klatte EC, Baehner R, Smith JA, Martin-Simmerman P, Carr BE, Provisor AJ, Weetman RM, Coates T, Siddiqui A, Weisman SJ, Berkow R, McKenna S, McGuire WA: Magnetic resonance imaging of bone marrow disease in children. Radiology 151:715–718, 1984.
11. Vogler JB, Murphy WA: Bone marrow imaging. Radiology 168:679–693, 1988.
12. Negendank W, Weissman D, Bey TM, de Planque MM, Karanes C, Smith MR, Ratanatharathorn V, Bishop CR, Al-Katib AM, Sensenbrenner LL: Evidence for clonal disease by magnetic resonance imaging in patients with hypoplastic marrow disorders. Blood 78:2872–2879, 1991.
13. Shah S, Ranade SS, Kasturi SR, Phadke RS, Advani SH: Distinction between normal and leukemic bone marrow by water protons nuclear magnetic resonance relaxation times. Magn Reson Imaging 1:23–28, 1982.
14. Moore SG, Gooding CA, Brasch RC, Ehman RL, Ringertz HG, Ablin AR, Matthay KK, Zoger S: Bone marrow in children with acute lymphocytic leukemia: MR relaxation times. Radiology 160:237–240, 1986.
15. Cohn J, Tygstrup I: Foamy histiocytosis of the spleen in patients with chronic thrombocytopenia. Scand J Haematol 16:33–37, 1976.
16. Luk SC, Musclow E, Simon GT: Platelet phagocytosis in the spleen of patients with idiopathic thrombocytopenic purpura (ITP). Histopathology 4:127–136, 1980.
17. Ishihara T, Akizuki S, Yokota T, Takahashi M, Uchino F, Matsumoto N: Foamy cells associated with platelet phagocytosis. Am J Pathol 114:104–111, 1984.
18. Fenaux P, Caulier MT, Hirschauer MC, Beuscart R, Goudemand J, Bauters F: Reevaluation of the prognostic factors for splenectomy in chronic idiopathic thrombocytopenic purpura (ITP). Eur J Haematol 42:259–264, 1989.
19. Siegel RS, Rae JL, Barth S, Coleman RE, Reba RC, Kurlander R,

Rosse WF: Platelet survival and turnover: Important factors in predicing response to splenectomy in immune thrombocytopenic purpura. Am J Hematol 30:206–212, 1989.
20. Kernoff LM, Malan E: Platelet antibody levels do not correlate with response to therapy in idiopathic thrombocytopenic purpura. Br J Haematol 53:559–562, 1983.
21. Najean Y, Dufour V, Rain JD, Toubert ME: The site of platelet destruction in thrombocytopenic purpura as a predictive index of the efficacy of splenectomy. Br J Haematol 79:271–276, 1991.
22. Lamy T, Moisan A, Dauriac C, Ghandour C, Morice P, Le Price PY: Splenectomy in idiopathic throbocytopenic purpura: Its correlation with the sequestration of autologous indium-111-labeled platelets. J Nucl Med 33:182–186, 1993.
23. Julia A, Araguas C, Rossello J, Bueno J, Domenech P, Olona M, Guardia R, Petit J, Flores A: Lack of clinical prectiors of response to splenectomy in patients with chronic idiopathic thrombocytopenic purpura. Br J Haematol 76:250–255, 1990.
24. Fujisawa K, Tani P, Piro L, McMillan R: The effect of therapy on platelet-associated autoantibody in chrnoic immune thrombocytopenic purpura. Blood 81:2872–2877, 1993.